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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

JIANG, DONG

ART UNIT

PAPER NUMBER

1646

MAIL DATE

DELIVERY MODE

10/21/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/584,805	Applicant(s) RUBINSTEIN ET AL.	
	Examiner DONG JIANG	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 August 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 31-67 is/are pending in the application.
- 4a) Of the above claim(s) 37-67 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 31-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 31-67 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 28 June 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/6/06</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED OFFICE ACTION

Applicant's election of Group I invention filed on 22 August 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Currently, claims 31-67 are pending. Claims 31-36 will be examined to the extent that they read on the elected invention. Claims 37-67 are withdrawn from further consideration as being drawn to a non-elected invention.

Formal Matters:

Information Disclosure Statement

Applicant's IDS submitted on 11/6/06 is acknowledged and has been considered. A signed copy is attached hereto.

Priority acknowledgement

This application is a national stage entry (371) of PCT/IL04/01170 with the international filing date of 12/27/04, which is acknowledged.

Specification

Title

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are directed.

Claims

Claims 34-36 are objected to for encompassing a non-elected subject matter: an expression vector (claims 34 and 35), or a cell that has been genetically modified (claim 36). The applicant is required to amend the claims to read only upon the elected invention.

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Claim 31 is objected to for the following informalities, appropriate correction is required for each item:

The claim recites “an antagonist/inhibitor of IL-1” in line 2, and it should be “an antagonist/inhibitor of IL-1” (i.e., a space is needed between “an” and “antagonist”).

Rejections under 35 U.S.C. §112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 31-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 31 is indefinite for the recitation of “a therapeutically effective amount” in lines 1-2 and line 4 because it is unclear for what it is therapeutically effective, and how the “therapeutically effective amount” can be determined, as there is no specific disease or condition recited, which could be treated with the said composition. The metes and bounds of the claim, therefore, cannot be determined. The claim is further indefinite for the recitation “*an antagonist/inhibitor of IL-1*, or a mutein, functional derivative, fraction, circularly permuted derivative, fused protein, isoform and a salt *thereof*” because it is unclear “thereof” what, since the claim does not define what “an antagonist/inhibitor of IL-1” is. Deletion of “or a mutein, functional derivative, fraction, circularly permuted derivative, fused protein, isoform and a salt thereof” would be remedial.

Claims 34-36 are similarly indefinite for the recitation of “a therapeutically effective amount”.

The remaining claims are included in this rejection because they are dependent from the specifically mentioned claims without resolving the indefiniteness issue belonging thereto.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

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art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, whatever is now claimed.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116).

Claim 31 recites “a mutein, functional derivative, fractions, circularly permuted derivative, fused protein, isoform and a salt thereof” of IL-18BP, which reads on any functional equivalent of IL-18BP. The specification merely teaches the use of human IL-18BP (Example 4, for example), and prior art has established that there are four specific isoforms of human IL-18BP resulted from alternative splicing, and only IL-18BP a and c isoforms have IL-18 neutralizing activity (Chvatchko et al., US2006/0233799, page 1, [0007]), and no IL-18BP variant of any kind, or any “functional equivalent” thereof meeting the limitations of the claim was ever identified or particularly described. The present claims encompass significant structural dissimilarity as compared to the IL-18BP, and the variants including functional equivalents without any sequence similarity required to the known IL-18BP. As such, a skilled artisan cannot envision the detailed chemical structure of the encompassed mutein, functional derivative, active fraction, or a circularly permuted derivative, and therefore conception is not achieved regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

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One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the IL-18BP, the functional isoforms, and the fusion protein thereof, but not the full breadth of the claims (muteins, functional derivative, fraction, and circularly permuted derivative) meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 31 and 34-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Sims et al., US 2002/0098185 A1 (7/25/02, provided by applicants).

Sims discloses the physiologically acceptable compositions of the IL-18 antagonist comprising soluble IL-18R or IL-18 binding protein in conjunction with physiologically acceptable carriers, excipients or diluents (page 5, [0046]). Further, Sims teaches methods for treating disorders characterized by elevated levels or abnormal expression of IL-18 by administering an IL-18 antagonist such as soluble IL-18R, an IL-18 binding protein and/or an antibody (abstract, for example), wherein the disorders include rheumatoid arthritis and IBD (claim 1, for example). Furthermore, Sims teaches that the various medical disorders as being treatable with an IL-18 antagonist are treated in combination with another cytokine or cytokine inhibitor, for example, IL-18 antagonist can be administered in a composition that also contains a compound inhibiting the interaction of other inflammatory cytokines with their receptors (page 6, [0052], lines 1-7), including the use of an IL-18 antagonist in combination with an IL-1

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antagonist (page 6, [0052], the last four lines of 1st column). Therefore, the reference anticipates the claims.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 32 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sims et al., US 2002/0098185 A1 (7/25/02, provided by applicants), as applied to claims 31 and 34-36 above, and further in view of Dombroski et al., US7,005,523.

The teachings of Sims are reviewed above. Sims does not specifically mention that the IL-1 antagonist is IL-1Ra or Kineret.

Dombroski teaches IL-1 inhibitors, including receptor antagonists or soluble IL-1ra (e.g. Kineret) or ICE inhibitors (column 15, lines 36-38), which can be used for the treatment of rheumatoid arthritis (column 15, lines 32-33).

Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to make a pharmaceutical composition comprising an antagonist/inhibitor of IL-1 such as Kineret and IL-18BP following the teachings by Sims and Dombroski. The person of ordinary skill in the art would have been motivated to do so for disease treatment such as rheumatoid arthritis as Sims and Dombroski teaches that both antagonist of IL-1 such as

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Kineret and an antagonist of IL-18 such as IL-18BP can be used for treating disorders such as rheumatoid arthritis, and reasonably would have expected success because both have been demonstrated to be able to inhibit IL-1 and IL-18, respectively.

Conclusion:

No claim is allowed.

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Advisory Information:

Any inquiry concerning this communication should be directed to Examiner Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Dong Jiang/, Ph.D.
Primary Examiner, Art Unit 1646
10/10/08